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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/650,726 | 08/29/2003 | Chihiro Uematsu | 1021.43085X00 | 9438 |

20457 7590 11/15/2005

ANTONELLI, TERRY, STOUT & KRAUS, LLP
1300 NORTH SEVENTEENTH STREET
SUITE 1800
ARLINGTON, VA 22209-3873

EXAMINER

BABIC, CHRISTOPHER M

ART UNIT PAPER NUMBER

1637

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|----------------------------------|--------------------------------|--|
| Office Action Summary | Application No. 10/650,726 | Applicant(s) UEMATSU ET AL. | |
| | Examiner Christopher M. Babic | Art Unit 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-11 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>8/29/03</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claims 1-5 have been cancelled. Claims 8-11 are pending. The following Office Action is in response to Applicant's response dated September 28, 2005. Any rejection set forth in the NON-FINAL Office Action dated June 28, 2005 not reasserted in the following Office Action is considered withdrawn. All rejections under 35 USC § 112, second paragraph, have been withdrawn in view of claim amendments. All rejections set forth in the following Office Action are considered necessitated by Applicant's amendment. The following Office Action is deemed **FINAL**.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Whitcombe et al. (WO 97/42345).

With regard to Claim 8, Whitcombe et al. disclose a gene expression analysis system wherein diagnostic primers having a tag region and detector region are practiced in a single tube genotyping method (Abstract; Page 1, Lines 20-23; **Figure 17(a), (b); Page 20, Example 1**, for example). They further disclose: (1) preparing first nucleotides including a targeted gene by using a first sample and introducing a first base sequence and a second base sequence (Figure 17, Allele A Specific, for example), which are nonspecific to the base sequence of the targeted gene to the targeted gene so that the second base sequence is bound to a position closer to the 5' end than is the first base sequence (Figure 17, Allele A Specific; Page 4, Lines 22-25); (2) preparing second nucleotides including the targeted gene by using a second sample and introducing a third base sequence and the second base sequence (Figure 17, Allele B Specific, for example), which are nonspecific to the base sequence of the targeted gene, to the targeted gene so that the second base sequence is bound to a position closer to the 5' end than is the third base sequence (Figure 17, Allele B Specific; Page 4, Lines 22-25); (3) subjecting the first nucleotides and the second nucleotides to nucleic acid amplification using a primer comprising a base sequence specifically hybridizing to the targeted gene (Figure 17 (a),(b); Page 4, Lines 22-25), a primer comprising a base sequence identical to the second base sequence (Figure 17 (a),(b)) , a first probe comprising a base sequence identical or complementary to the first base sequence (Figure 17, Allele A Specific), and labeled at one end with a first fluorophore and at another end with a quencher (Figure 17; Page 2, Lines 23-29), a second probe comprising a base sequence identical or complementary to the third base sequence

(Figure 17, Allele B Specific), and labeled at one end with a second fluorophore and at another end with a quencher (Figure 17; Page 2, Lines 23-29), and thermostable DNA polymerase having 5'-3' exonuclease activity (Page 2, Lines 23-29, i.e. FRET); (4) digesting the first probe and the second probe bound to the first base sequence and the third base sequence, by the thermostable DNA polymerase at the time of the nucleic acid amplification (Page 2, Lines 23-29, i.e. FRET) ; (5) and detecting a fluorescence emitted by the first fluorophore and the second fluorophore released in digesting the first probe and the second probe, thereby assaying the amount of the product of the nucleic acid amplification (Page 2, Lines 23-29, i.e. FRET; Page 19, Lines 5-12, for example).

With regard to Claim 9, Whitcombe et al. disclose diagnostic primers which are genome specific at their 3'-termini (i.e. "fourth base sequence") but which carry detector region and common extension tags (tags) at their 5'-termini (Page 4, Lines 22-25; Figure 17, for example).

With regard to Claim 10, Whitcombe et al. disclose that the nucleic acid sample may be DNA, RNA or reverse transcribed RNA (i.e. cDNA) (Page 9, Line 30-Page 10, Line 2).

Furthermore, Whitcombe et al. disclose their invention as being well suited for homogeneous assays and real time or end point analysis (Page 2, Lines 17-18). It is inherent to one of ordinary skill in the art that "real time or end point analysis" encompasses quantification of mRNA by using a reverse transcriptase PCR reaction to prepare cDNA for experimentation (For example, please see included reference: Overbergh et al. (Quantification of Murine Cytokine mRNAs Using Real Time

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Quantitative Reverse Transcriptase PCR. Cytokine, Vol. 11, No. 4. April, 1999: 305-312)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al. (WO 97/42345), in view of Shah et al. (U.S. 6,165,723).

With regard to Claim 5, the methods disclosed by Whitcombe et al. are outlined in the above rejections. Whitcombe et al. does not specifically teach a multiplex assay with multiple probes having substantially the same T_m value.

Shah et al. disclose an in situ hybridization method for detecting target nucleic acids, wherein for simultaneous detection the oligonucleotides which are specific for the different nucleic acids commonly present in the clinical specimen can be designed such that the T_m values of all probe complex sequences are very similar (Abstract; Column 5, Lines 1-18). In addition, Shah et al. disclose several advantages of their methods, such as reduction hybridization time (Column 5, Lines 58-67).

One of ordinary skill in the art would have been motivated to use the probes disclosed by Shah et al. in the diagnostic amplification methods disclosed by Whitcombe et al. for among other advantages, a reduction in hybridization time. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

Conclusion

No claims are allowed. No claims are free of the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

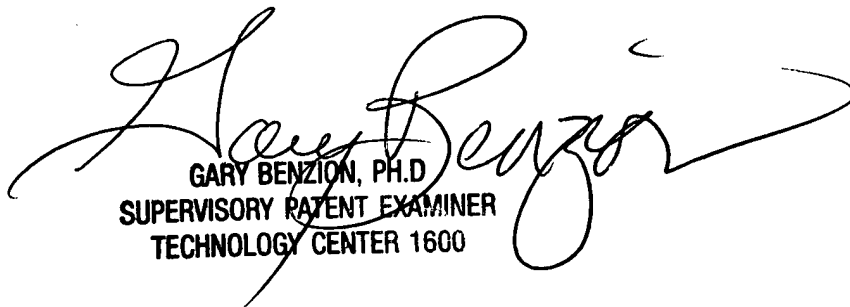
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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

 11/7/05

Christopher M. Babic
Patent Examiner
AU 1637



GARY BENZION, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600